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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,367	02/26/2004	Michael Graupe	USAV2001/0143 US CNT	7957

46137 7590 07/12/2005

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,367	GRAUPE ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *1-16 in part* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12* is/are rejected.

7)☒ Claim(s) *1-9 and 13-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 pending in the instant application.

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on application PCT/US02/29323. It is noted, however, that applicant has not filed a certified copy of the PCT application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

2. Applicant's Information Disclosure Statement (IDS), filed May 18, 2005, has been considered by the Examiner. Please refer to the signed copy of Applicant's PTO-1449 form submitted herewith.

Election/Restrictions

3. Applicant's election **with traverse** of Group I, claims 1-16, in part, wherein X^3 is a group of formula (a), is acknowledged.

Regarding the traversal, the Examiner directs Applicants' attention to Section 803.02 of the MPEP, the subsection that addresses Markush-type claims:

> "This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, the examiner may require a provisional election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn

from further consideration."

Therefore, the claims herein lack unity of invention under MPEP 803.02, since the compounds defined in the claims lack a significant structural element qualifying as the substantial structural feature that defines a contribution over the prior art. The compounds claimed contain only an amino-alkyl-sulfonyl moiety in common (variables **excluded**), referred to as "the backbone" in page 5 of Applicants' Response, which does not define a contribution over the prior art. Please refer to the referenced Chapman et al patent, U.S. 5,672,583, which discloses the same basic backbone. Furthermore, the substituents vary extensively and when taken as a whole result in vastly different compounds. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Additionally, the vastness of the claimed subject matter and the complications in understanding the claimed subject matter imposes a burden on any examination of the claimed subject matter.

The requirement is still deemed proper and is therefore made FINAL.

4. Accordingly, Groups II and III, drawn to claims 1-16 in part, wherein X^3 is a group of formula (b) or (c), currently withdrawn from consideration pursuant to 37 CFR 1.142(b), as directed to non-elected subject matter.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 11 and 12 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 11 rejected under 35 U.S.C. 112 as being an *improper product-use* claim. The claim provides for "The use of a compound..." but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

(b) Claim 12 rejected under 35 U.S.C. 112, since steps (D)-(J) are confusing. Even though each step is labeled "optionally," it is unclear if the steps are meant to be consecutive, or if only one of steps (D)-(J) is actually intended for the process. It is also unclear as to how each is carried out, i.e. there are no descriptions provided for the individual steps such that reaction conditions, solvent use, parameters, etc have been omitted from the claim. Clarification is requested.

The Examiner also reminds Applicant that method claims 10-12 have only been examined to the extent that they correspond to the scope of Group I, as stated in the Restriction Requirement.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 10 and 11 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While various diseases/disorders may be listed in the specification, the claims are not

enabled for *all* disorders responsive to the inhibition of Cathepsin S, since there is no indication as to the full range of disorders that could be treated using the instant claimed method.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the claims are directed to many disorders and conditions that are not enabled in the specification, including those broadly recited in claims 10 and 11.

The nature of the invention

The nature of the invention is the inhibition of Cathepsin S, comprising administering the instant claimed compound to a subject in need thereof. However, claims 10 and 11 are reach-through claims, drafted in terms of inhibiting a cellular event, which is not a specific utility such that one skilled in the art would know how to perform the claimed method for treating a specific disease or diseases.

The state of the prior art and the predictability or lack thereof in the art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of

ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence of a showing of correlation between *all* the diseases alleged as capable of being treated by the compound of the instant claims and the response of Cathepsin S activity, one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds.

The amount of direction or guidance present and

the presence or absence of working examples

Treatment of diseases/disorders are normally disease or symptom oriented, thus are highly individualized. Applicants have not demonstrated that inhibiting the biochemical pathway of Cathepsin S and treating the many diseases/ disorders described in the specification and encompassed by claims 10 and 11are inexorably linked. The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. The specification also only discusses a few basic compounds in four *in vitro* assays which describe their inhibition constants on pages 70-72, and provide no data for describing the efficacy of the claimed compounds for treating the full scope of disorders that Applicants have pointed out on pages 34-35 of the specification.

The breadth of the claims

Applicants are claiming a method of inhibiting Cathepsin S, alleging that said method encompasses a broad number of diseases or conditions, including autoimmune disorders, allergic disorders, allogeneic immune responses, elastolysis disorders, cardiovascular disease, as well as systemic amyloidosis. The argument that the diseases claimed by the Applicants are all treated by inhibiting Cathepsin S is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the disorders and conditions encompassed by

the broadly recited claims 10 and 11.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every disease/condition encompassed by claims 10 and 11, using the instant claimed compounds. One of skill in the art would need to determine what diseases would be benefited by inhibiting Cathepsin S and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the disorders and conditions by said activity. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds not only inhibit the activity of a chemokine, but also treat disorders of real-world relevance.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The Examiner suggests claiming the possible diseases and conditions that are treated, rather than claiming the mechanism, which is speculative, and recommends the following language, "A method of inhibiting Cathepsin S, for treating asthma, COPD, and bronchiolitis, (to name few)... comprising administering to a patient in need thereof, a therapeutically effective amount of a compound of Claim 1...."

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 11 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Objections

11. Claims 1-9 and 13-16 currently objected to as containing non-elected subject matter.

Conclusion

12. Claims 1-16 are pending in the application, claims 1-16 wherein X^3 is (b) or (c) are currently withdrawn from consideration, claims 10-12 stand rejected, and claims 1-9 and 13-16 are objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
July 5, 2005

Joseph K. McKane
SPE, Art Unit 1626